ION MOBILITY MEASUREMENT AT A POTENTIAL BARRIER

BACKGROUND

The invention relates to measurements of ion mobilities in gases under the influence of electric fields. Mass spectrometers can only ever determine the ratio of the ion mass to the charge of the ion. In the following, the term "mass of an ion" or "ion mass", which is used for the sake of simplicity, always refers to the ratio of the mass m to the number of elementary charges z of the ion. This charge-related mass m/z has the physical dimension of a mass; it is often called "mass-to-charge ratio", although this is dimensionally incorrect. "Ion species" shall denote those ions having the same elementary composition, the same charge and the same structure. The ion species generally comprises all the ions of an isotope group, which may well include ions of slightly different masses, but virtually the same mobilities.

Isomers of the primary structure of bioorganic molecules (structural isomers) and isomers of the secondary or tertiary structure (conformational isomers) show different geometrical forms but exactly the same mass. It is therefore impossible to differentiate between them on the basis of their mass alone. Some information as to the structure can be obtained from fragment ion spectra; however, an efficient and certain way to recognize and distinguish such isomers is to separate them according to their different ion mobilities.

Today, ion mobilities are predominantly measured via the drift velocities of the ions in long drift regions. A drift region for measuring ion mobility contains an inert gas (such as helium or nitrogen). The ions of the substance under investigation are pulled through the gas by means of an electric field produced by suitable DC potentials at ring electrodes, which line the drift region. The large number of collisions with the gas molecules produces a constant drift velocity v_d for each ion species which is, in first approximation, proportional to the electric field strength E: $v_d = K_0 \times E$. The proportionality constant K_0 is called the "ion mobility" of this ion species. The ion mobility is a function of the temperature, gas pressure, type of gas, ion charge and, in particular, the collision cross-section of the ions. At the same temperature, pressure and type of gas, isomeric ions of the same charge-related mass m/z, but different collision cross-sections have different ion mobilities. Isomers of the smallest geometric dimension possess the greatest mobility and therefore the highest drift velocity through the gas. Unfolded protein ions undergo more collisions than tightly folded proteins. Protein ions which are unfolded, or partially folded, therefore arrive at the end of the cell later than strongly folded ions of the same mass. But structural isomers, for example proteins with glycosyl, lipid or phosphoryl groups at varying sites, also have different collision cross-sections, which allows them to be distinguished by measuring their ion mobility.

In modern chemical and biological research, it has become more and more important to have knowledge about the folding structures of molecules, which often can be determined by mobility measurements of their ions. Therefore devices to measure the mobility of ions have been incorporated into mass spectrometers, in particular to combine measurement of the charge-related mass of ions with measurement of collision cross-sections. The folding structures strongly influence the mechanism of action and thus the effect of the molecules in the living organism; different foldings can signify normal or abnormal functions of biopolymers in biosystems, and hence health or disease of tissue parts of even whole organisms.

A variety of information can be obtained from ion mobility measurement. It is possible to qualitatively detect simply the existence of different conformational isomers, for example. More detailed measurements of the mobility spectra can be used to quantitatively analyze mixtures of structural isomers or conformational isomers (as part of quality control for the production of chemicals, for example). Folding patterns can be confirmed or disproved by calibrated ion mobility measurements with determination of exact mobility values and comparisons with computed collision cross-sections.

A number of academic research groups have coupled ion mobility spectrometry with mass spectrometers. A pressure range of a few hectopascals has been adopted almost universally for the mobility drift region; the drift region for higher mobility resolutions is up to four meters and more, and electric field strengths of 2,000 volts per meter and more are applied. In this pressure range, the drifting ions appear to form hardly any complexes with other substances, so the mobilities of the ion species can be measured without any interference, unlike mobility measurements at atmospheric pressure. But in the long drift regions, the ions also diffuse radially over long distances, and therefore quite large diameters have to be chosen for these drift regions.

The ions are usually introduced into the drift region in the form of temporally short ion pulses, as a result of which they initially adopt the shape of spatially small ion clouds, which are pulled through the drift region by the electric field. In the gas of the drift region, these ion clouds are subject to diffusion into the surrounding space, the diffusion being caused by collisions statistically distributed in terms of spatial directions and kinetic energies due to molecular Brownian motion. The diffusion takes place in both the forward and the backward direction, and also at right angles to the drift region. The gas in the drift region is often kept at temperatures of between about 150 and 300 degrees Celsius, but can also be greatly cooled for special experiments. The mobility resolving power R_{mob} ("mobility resolution" for short) is influenced predominantly by this diffusion broadening of the ion clouds, especially for long drift regions and high electric field strengths; all other influences, such as the space charge, are negligibly small. The part of the mobility resolution determined by the diffusion broadening is given by the equation

$$R_d = \sqrt{\frac{zeEL_d}{kT \ln 2}},$$

where z is the number of elementary charges e, E the electric field strength, L_d the length of the drift region, k the Boltzmann constant and T the temperature of the gas in the drift region. The mobility resolution is defined as $R_{mob} = K_0/\Delta K_0$, where ΔK_0 is the width of the ion signal of the mobility K_0 at half height, measured in units of the mobility. The part R_d of the mobility resolution given by the diffusion is not dependent on either the type or pressure of the gas in the drift region; the mobility K_0 itself, however, does depend not only on the temperature, but also on the pressure and type of the gas.

As is known from very early work on charged particles from the end of the 19th century, this type of ion mobility measurement in a non-moving drift gas can be modified by a counter-flow of the gas in the drift region, resulting in a shortening of the drift region. In this case, arbitrarily high mobility resolutions can, in theory, be achieved for ions of a selected mobility, which are held over a long period in equilibrium between the electric force of attraction and the viscous drag in the gas; but unfortunately only in theory. For